## REMARKS

Applicants respectfully request reconsideration of the present application.

### I. Amendments to the Specification

In the specification, the following paragraphs have been amended to overcome the trademark-capitalization-objection: 26-27, 52, 54-55, & 61. Office action, pp. 2-3. Each objection should be withdrawn.

### II. Disposition of the claims

Claims 1-12 are pending. No claim is canceled. Claim 9 is currently amended to correct a pair of inadvertent typographical errors. No claim is new.

This amendment adds, changes and/or deletes claims in this application. A detailed listing of all claims that are, or were, in the application, irrespective of whether the claim(s) remain under examination in the application, is presented, with an appropriate status identifier.

### III. Claim objection

Claim 9 was objected to for containing misspellings, which were corrected. The Examiner is thanked and asked to withdraw the objection.

### IV. Obviousness rejection

#### A. Specific comments traversing this rejection

Claims 1-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Menzi et al. (6,056,949), in view of Nissenson et al. (The Western Journal of Medicine, 1979, 13 1, pp. 277-284), Debregeas et al. (4,960,596), De Long et al. (6,030,621) and DeBregeas et al. (U.S. Patent No. 6,228,395). Office action, p. 4. The Examiner states that "Menzi et al. do not teach mannitol specifically," Office action, p. 5, but urged that mannitol is known, Office action p. 5

("Nissenson et al., teach mannitol is made from the carbohydrate, or sugar, dextrose (p. 277)."), and that a sugar is a sugar regardless of its type:

> Mannitol is a modified sugar and as such, it is reasonably expected that a composition of any sugar, e.g. sucrose from the composition of Menzi et al., would yield the same composition comprising a sugar substance as recited in the instant claim 2 [which recites mannitol by name].

Office action, p. 5 (emphasis added). Without proceeding further, it is plain to see why this rejection is improper.

The Examiner has held that the restriction requirement was deemed proper and final. Office action, p. 2. In other words, the Examiner finally held that each combination of elected species is patentably distinct. Restriction Requirement, pp. 2-3. For example, the Examiner clearly stated that that each elected species is patentably distinct:

> Should applicant traverse on the ground that the inventions or species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the inventions or species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C.103(a) of the other invention.

Restriction Requirement, p. 3 (emphasis added), and that a search would be a serious burden:

> It is noted that the species of a neutral core and the species of plant substances are structurally distinct and the search for each neutral core and the search for each plant substance would represent an undue burden on the Office. The neutral core may be selected from, for example, sugar, starch, mannitol, sorbitol, xylitol, cellulose, or talc. The plant substance may be selected from, for example, garlic, Ginkgo biloba, ginseng, Harpagpphytum, St. John's wort, green tea, valerian, or Orthosiphon.

Restriction Requirement, p. 2 (emphasis added).

The restriction requirement and the present rejection are contradictory. On one page, the Examiner effectively states that each pair of "neutral core" and "plant substances" is patentably distinct. On a subsequent page, the Examiner states that one neutral core is fungible with another. The Examiner cannot play both sides of the issue, or in legalese, the rejection is not supported by substantial evidence.

The remaining references were not applied to remedy these deficiencies. As such, the rejection is improper and should be withdrawn.

B. **General comments about maintaining this obviousness rejection.**

If the Examiner maintains the obviousness rejection in its present form, then it may be construed that the Examiner is refusing to examine the claims as was done in, e.g., In re Haas, 580 F.2d 461, 464, 198 USPQ 334, 336 (CCPA 1978).

## V. Obviousness Double Patenting (ODP) Rejections

There are two sets of ODP rejections. Each set is addressed under a separate header.

### A. Set A

Claims 1 and 12 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 5 of Debregeas et al. (5,385,739), claim 21 of Leduc et al. (5,549,911), claims 13 and 21 of Debregeas et al. (6,077,544), claims 17, 25, and 26 of Debregeas et al. (6,139,877), claims 17,25, and 26 of Debregeas et al. (6,458,389), claim 10 of Debregeas et al. (6,482,437), claim 14 of Debregeas et al. (6,55 1,621), and claim 1 of Debregeas et al. (6,770,298). Office action, p. 7. The rejection reads as follows:

> Although the conflicting claims are not identical, they are not patentably distinct from each other because the above claims of each of the Debregeas et al. patents and claim 21 of Leduc et al. are directed at granules, which is the same granules used in granules in the instant claims 1 and 12. Thus the granules are not patentably

> distinct between each of the Debregeas et al. patents and the instant application.

Office action, pp. 7-8 (emphasis added).

The Examiner's argument is contradictory. How could the subject matter be the "same" but "not identical" at the same time? Each rejection should be withdrawn for this reason alone.

Each rejection is further traversed under a separate header.

***1. Over claim 5 of Debregeas et al. (5,385,739)***

Claims 1 and 5 of the '739 patent read as follows:

> 1. A stable formulation of omeprazole microgranules containing a neutral core of sugar and starch and an active layer consisting of a dilution of omeprazole in mannitol in substantially equal amounts, wherein the active omeprazole layer contains about 10% by weight of carboxymethylstarch, about 5% by weight of a sodium lauryl sulfate surface-active compound, and wherein the dilution of omeprazole in mannitol is applied to the neutral core by means of hydroxypropyl methylcellulose as a high viscosity binder.
>
> 5. A process for producing the formulations as claimed in claim 1, wherein a dry dilution of mannitol and of omeprazole is applied to neutral grains consisting of sugar and of starch with the aid of a high-viscosity binding solution of hydroxypropyl methylcellulose in solution in a mixture of at least 80% ethanol and at most 20% water.

Here, the Examiner has not met her initial burden of establishing a prima facie case of ODP, Cf. In re Oetiker, 977 F.2d 1443, 1445, 24 U.S.P.Q.2d 1443, 1444 (Fed. Cir. 1992), because the Examiner ignores claim elements. For example, the rejection does not even attempt to liken the cited claims to the recited structure of rejected claims 1 and 12, let alone citing evidence and explaining the rejection. As such, the rejection is improper and should be withdrawn.

*2. Over claim 21 of Leduc et al. (5,549,911)*

Claims 1 and 21 of the '911 patent read as follows:

> 1. Galenic form of 5-nitroimidazole derivatives characterized in that it comprises a combination of microgranules of 5-nitroimidazole derivatives consisting of gastroresistant microgranules and prolonged-release microgranules.
>
> 21. A process of treating infections of the gastrointestinal tract of an animal comprising administering the galenic form of the compound of claim 1 to the animal.

Here, the Examiner has not met her initial burden of establishing a prima facie case of ODP, Cf. In re Oetiker, 977 F.2d 1443, 1445, 24 U.S.P.Q.2d 1443, 1444 (Fed. Cir. 1992), because the Examiner ignores claim elements. For example, the rejection does not even attempt to liken the cited claims to the recited structure of rejected claims 1 and 12, let alone citing evidence and explaining the rejection. As such, the rejection is improper and should be withdrawn.

*3. Over claims 13 and 21 of Debregeas et al. (6,077,544)*

Claims 1, 7, 13, and 21 of the '544 patent read as follows:

> 1. Spheroids comprising one or more active principles, with the exception of tiagabine, wherein said spheroids further comprise:
>
> a core and a layer coating said core, wherein said layer comprises at least one thermoplastic excipient which is of pasty to semi-solid consistency at a temperature of about 20° C., and whose melting point is between about 25 ° C. and about 100 ° C., coated with
>
> a flexible and deformable film, based on a polymer material, which ensures either protection or masking of the taste, or modified and controlled release of said one or more active principles, wherein said spheroids can be compressed directly without the addition of a substantial part of an auxiliary substance.

> 7. Spheroids according to claim 1, wherein said spheroids are coated with a water-dispersible outer layer which provides said spheroids with cohesion during a compression step and which ensures breakdown in aqueous medium of the tablet obtained.
>
> 13. A process for the preparation of the spheroids according to claim 1, wherein said layer containing at least one thermoplastic excipient and said film containing a polymer material are successively deposited on the cores by spraying, in a granulating turbomixer, in a perforated turbomixer, or in a fluidized-air bed.
>
> 21. A process for the preparation of spheroids according to claim 7, wherein said layer containing at least one thermoplastic excipient, said film containing a polymer material, and said outer layer are successively deposited on the cores by spraying, in a granulating turbomixer, in a perforated turbomixer, or in a fluidized-air bed.

Here, the Examiner has not met her initial burden of establishing a prima facie case of ODP, Cf. In re Oetiker, 977 F.2d 1443, 1445, 24 U.S.P.Q.2d 1443, 1444 (Fed. Cir. 1992), because the Examiner ignores claim elements. For example, the rejection does not even attempt to liken the cited claims to the recited structure of claims 1 and 12, let alone citing evidence and explaining the rejection. As such, the rejection is improper and should be withdrawn.

***4. Over claims 17, 25, and 26 of Debregeas et al. (6,139,877)***

Claims 1, 14, and 17 of the '877 patent read as follows:

> 1. Spheroids containing tiagabine as active principle and comprising:
>
> a core, or
>
> a core coated with a layer, said layer containing at least one thermoplastic excipient which is of pasty to semi-solid consistency at a temperature of about 20° C., and whose melting point is between about 25° C. and about 100° C.,
>
> said core or said layer being coated with

> a flexible and deformable film, based on a polymer material, whose glass transition temperature is less than about 30° C., which ensures either protection or masking of the taste, or modified and controlled release of the tiagabine.
>
> 14. Multiparticulate pharmaceutical preparations containing the spheroids according to claim 1.
>
> 17. Pharmaceutical preparations according to claim 14, wherein said pharmaceutical preparations are in the form of tablets of said spheroids.

Claims 25-26 are not in the '877 patent.

Here, the Examiner has not met her initial burden of establishing a prima facie case of ODP, Cf. In re Oetiker, 977 F.2d 1443, 1445, 24 U.S.P.Q.2d 1443, 1444 (Fed. Cir. 1992), because the Examiner ignores claim elements. For example, the rejection does not even attempt to liken the cited claims to the recited structure of claims 1 and 12, let alone citing evidence and explaining the rejection. As such, the rejection is improper and should be withdrawn.

***5. Over claims 17, 25, and 26 of Debregeas et al. (6,458,389)***

Claims 1, 17, and 25-26 read as follows:

> 1. Controlled-release microgranules comprising (1) (a) a mixture comprising cisplatin and at least one pharmaceutically acceptable excipient or (b) a core of a neutral support grain coated with a mixture comprising cisplatin and at least one pharmaceutically acceptable excipient; and (2) a coating fixed to the microgranule, wherein the coating comprises a coating agent which enables the controlled release of the mixture; wherein the microgranules have a mean particle size of between 0.4 and 1.5 mm; and wherein the microganules contain only cisplatin as an active ingredient.
>
> 17. A process for preparing the microgranules of claim 1, which comprises spraying cisplatin in a suspension medium onto a neutral support grain to form microgranules, and then fixing a coating to the microgranules, wherein the suspension medium is water, an alcohol, or a water-alcohol mixture.

> 25. A method for manufacturing an oral medicament, comprising preparing microgranules according to claim 1 and formulating an oral medicament comprising said microgranules.
>
> 26. A method for treating cancer comprising administering to a subject in need thereof the oral medicament according to claim 25 at a daily cisplatin dosage of not more than 20 $mg/m^2$.

Here, the Examiner has not met her initial burden of establishing a prima facie case of ODP, Cf. In re Oetiker, 977 F.2d 1443, 1445, 24 U.S.P.Q.2d 1443, 1444 (Fed. Cir. 1992), because the Examiner ignores claim elements. For example, the rejection does not even attempt to liken the cited claims to the recited structure of claims 1 and 12, let alone citing evidence and explaining the rejection. As such, the rejection is improper and should be withdrawn.

***6. Over claim 10 of Debregeas et al. (6,482,437)***

Claims 1 and 10 of the '437 patent read as follows:

> 1. An immediate-release microganule, each microgranule comprising a neutral support grain coated with a mixture of morphine sulfate and of a pharmaceutically acceptable binder, said binder representing 10 to 50% by weight of the morphine sulfate/binder mixture, and wherein said microgranule has a dissolution profile in water, buffered at a pH approximately equal to 7 and at a temperature of 37° C., by dissolution with a paddle at 100 revolutions/min, such that: more than 70% by weight of active principle is dissolved after 30 minutes, more than 90% by weight of active principle is dissolved after 60 minutes.
>
> 10. A process for the preparation of the microgranule as claimed in claim 1, which is carried out entirely in aqueous medium.

Here, the Examiner has not met her initial burden of establishing a prima facie case of ODP, Cf. In re Oetiker, 977 F.2d 1443, 1445, 24 U.S.P.Q.2d 1443, 1444 (Fed. Cir. 1992), because the Examiner ignores claim elements. For example, the rejection does not even attempt to liken the cited claims to the recited structure of claims 1 and 12, let alone citing evidence and explaining the rejection. As such, the rejection is improper and should be withdrawn.

*7. Over claim 14 of Debregeas et al. (6,551,621)*

Claims 1, 6, and 14 of the '621 patent read as follows:

> 1. Omeprazole microgranules, each comprising an active layer comprising the active principle and an external gastroprotective layer comprising a gastroprotective agent, characterized in that they are devoid of alkaline compounds in the form of salts and that the active layer comprises a hydrophobic substance.
>
> 6. Microgranules, wherein each microgranule comprises (A) a layer of active principle comprising omeprazole, a binder chosen from any pharmaceutically acceptable binder, a hydrophobic substance and a solubilizing substance; (B) a first protective layer comprising one or more pharmaceutically acceptable diluent substances and a binder; (C) a second hydrophobic protective layer comprising a coating agent and a hydrophobic plasticizer; and (D) a gastroprotective layer comprising an enteric film-forming agent, a plasticizer, and a hydrophobic substance.
>
> 14. A process for the preparation of the microgranules as claimed in claim 1 or 6, wherein the process is carried out in aqueous medium.

Here, the Examiner has not met her initial burden of establishing a prima facie case of ODP, Cf. In re Oetiker, 977 F.2d 1443, 1445, 24 U.S.P.Q.2d 1443, 1444 (Fed. Cir. 1992), because the Examiner ignores claim elements. For example, the rejection does not even attempt to liken the cited claims to the recited structure of claims 1 and 12, let alone citing evidence and explaining the rejection. As such, the rejection is improper and should be withdrawn.

*8. Over claim 1 of Debregeas et al. (6,770,298)*

Claim 1 of the '298 patent reads as follows:

> 1. A device for producing granules comprising a drum with peripheral apertures, a member for feeding said drum with coating or fixing substance, and a member for supplying gas, wherein said peripheral apertures are defined by the space between mutually parallel sections contained in said drum and, wherein a gas passes

through said peripheral apertures between the inside and the outside of said drum.

Here, the Examiner has not met her initial burden of establishing a prima facie case of ODP, Cf. In re Oetiker, 977 F.2d 1443, 1445, 24 U.S.P.Q.2d 1443, 1444 (Fed. Cir. 1992), because the Examiner ignores claim elements. For example, the rejection does not even attempt to liken the cited claims to the recited structure of claims 1 and 12, let alone citing evidence and explaining the rejection. As such, the rejection is improper and should be withdrawn.

B. **Set B.**

Claims 1 and 12 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 1 of Debregeas et al. (4,960,596), claims 1, 10, and 18 of Debregeas et al. (Re. 35,903), claim 1 of Debregeas et al. (5,385,739), claim 1 of Leduc et al. (5,549,91 l), claim 1 of Debregeas et al. (6,077,544), claim 1 of Debregeas et al. (6,139,877), claim 1 of DeBregeas et al. (6,228,395), claim 1 of Debregeas et al. (6,383,516), claim 1 of Debregeas et al. (6,458,389), claim 1 of Debregeas et al. (6,482,437), claim 1 of Debregeas et al. (6,551,621), and claim 1 of Debregeas et al. (6,660,296) in view of Menzi et al. (6,056,949), Nissenson et al. (The Western Journal of Medicine, 1979, 13 1, pp. 277-284), Debregeas et al. (4,960,596), De Long et al. (6,030,621) and DeBregeas et al. (U.S. Patent 6,228,395) as applied to claims 1-12 above.

None of the cited primary patents remedies the deficiencies of the obviousness rejection, noted above, which rejection applied the teachings of the secondary references. As such, each of the present rejections should be withdrawn for this reason alone.

Each rejection is further traversed under a separately enumerated header.

*1. Over claim 1 of Debregeas et al. (4,960,596)*

Claim 1 of the '596 patent reads as follows:

> 1. A slow release acid-free Galenical preparation of pharmaceutically acceptable Diltiazem comprising microgranules of the type constituted by a central core coated with layers containing the active substance, with each microgranule having an outer membrane, the preparation being wherein its outer membrane is adapted to release the Diltiazem applied to the neutral core into an aqueous medium at the following rate measured using the method of the United States Pharmacopeia No. 21:
>
> (a) between 5% and 35% after one hour;
>
> (b) between 15% and 40% after two hours;
>
> (c) between 20% and 50% after three hours;
>
> (d) between 30% and 75% after four hours;
>
> (e) between 40% and 80% after six hours;
>
> (f) between 55% and 95% after eight hours whereas said preparation, comprises, relative to the total weight of microgranules, 8% to 15% by weight of neutral core, layers of diltiazem comprising 60% to 85% by weight mixed with polyvinylpyrrolidone comprising 8% to 15% by weight, 0.1% to 10% by weight talc and 1% to 20% by weight outer membrane, and wherein the outer membrane comprises by weight of total microgranule weight, 2% to 5% shellac, 1% to 15% by weight ethylcellulose and 0.17to 4% by weight of plasticizer.

It was canceled during a reissue, *vide infra*. As such, the rejection should be withdrawn.

Furthermore, the Examiner has not met her initial burden of establishing a prima facie case of ODP, Cf. In re Oetiker, 977 F.2d 1443, 1445, 24 U.S.P.Q.2d 1443, 1444 (Fed. Cir. 1992), because the Examiner ignores claim elements. For example, the rejection does not even attempt to liken the cited claims to the recited structure of claims 1 and 12, let alone citing evidence and explaining the rejection. As such, the rejection is improper and should be withdrawn.

*2. Over claims 1, 10, and 18 of Debregeas et al. (Re. 35,903)*

This patent is the reissue of the '596 patent. Claims 1, 10, and 18 of the '903 patent read as follows:

> 1. Canceled.
>
> 10. A slow release acid-free Galenical preparation of pharmaceutically acceptable Diltiazem comprising microgranules of the type constituted by a central core coated with layers containing the active substance, with each microgranule having an outer membrane, the preparation being wherein its outer membrane is adapted to release the Diltiazem applied to the neutral core into an aqueous medium at the following rates measured using the method of the United States Pharmacopeia No. 21:
>
> (a) between 5% and 35% after one hour;
>
> (b) between 15% and 40% after two hours;
>
> (c) between 20% and 50% after three hours;
>
> (d) between 30% and 75% after four hours;
>
> (e) between 40% and 80% after six hours;
>
> (f) between 55% and 95% after eight hours whereas said preparation comprises, relative to the total weight of microgranules, 8% to 15% by weight of neutral core, layers of Diltiazem comprising 60% to 85% by weight mixed with polyvinylpyrrolidone comprising 4% to 6% by weight, and 1% to 20% by weight outer membrane wherein the outer membrane includes, expressed in terms of total microgranule weight, 2% to 5% shellac and 1% to 3% ethylcellulose and 0% to 10% talc.
>
> 18. A slow release acid-free Galenical preparation of pharmaceutically acceptable Diltiazem comprising microgranules of the type constituted by a central core coated with layers containing the active substance, with each microgranule having an outer membrane, the preparation being wherein its outer membrane is adapted to release the Diltiazem applied to the neutral core into

> an aqueous medium at the following rates measured using the method of the United States Pharmacopeia No. 21:
>
> (a) between 5% and 35% after one hour;
>
> (b) between 15% and 40% after two hours;
>
> (c) between 20% and 50% after three hours;
>
> (d) between 30% and 75% after four hours;
>
> (e) between 40% and 80% after six hours;
>
> (f) between 55% and 95% after eight hours whereas said preparation comprises, relative to the total weight of microgranules, 8% to 15% by weight of neutral core, layers of Diltiazem comprising 60% to 85% by weight mixed with polyvinylpyrrolidone comprising 4% to 6% by weight, and 1% to 20% by weight outer membrane, wherein the outer membrane includes, expressed in terms of total microgranule weight, 1% to 15% by weight ethylcellulose and 0.4% to 4% by weight plasticizer.

Here, the Examiner has not met her initial burden of establishing a prima facie case of ODP, Cf. In re Oetiker, 977 F.2d 1443, 1445, 24 U.S.P.Q.2d 1443, 1444 (Fed. Cir. 1992), because the Examiner ignores claim elements. For example, the rejection does not even attempt to liken the cited claims to the recited structure of claims 1 and 12, let alone citing evidence and explaining the rejection. As such, the rejection is improper and should be withdrawn.

### *3. Over claim 1 of Debregeas et al. (5,385,739)*

Claim 1 of the '739 patent reads as follows:

> 1. A stable formulation of omeprazole microgranules containing a neutral core of sugar and starch and an active layer consisting of a dilution of omeprazole in mannitol in substantially equal amounts, wherein the active omeprazole layer contains about 10% by weight of carboxymethylstarch, about 5% by weight of a sodium lauryl sulfate surface-active compound, and wherein the dilution of

> omeprazole in mannitol is applied to the neutral core by means of hydroxypropyl methylcellulose as a high viscosity binder.

Here, the Examiner has not met her initial burden of establishing a prima facie case of ODP, Cf. In re Oetiker, 977 F.2d 1443, 1445, 24 U.S.P.Q.2d 1443, 1444 (Fed. Cir. 1992), because the Examiner ignores claim elements. For example, the rejection does not even attempt to liken the cited claims to the recited structure of claims 1 and 12, let alone citing evidence and explaining the rejection. As such, the rejection is improper and should be withdrawn.

***4. Over claim 1 of Leduc et al. (5,549,911)***

Claim 1 of the '911 patent reads as follows:

> 1. Galenic form of 5-nitroimidazole derivatives characterized in that it comprises a combination of microgranules of 5-nitroimidazole derivatives consisting of gastroresistant microgranules and prolonged-release microgranules.

Here, the Examiner has not met her initial burden of establishing a prima facie case of ODP, Cf. In re Oetiker, 977 F.2d 1443, 1445, 24 U.S.P.Q.2d 1443, 1444 (Fed. Cir. 1992), because the Examiner ignores claim elements. For example, the rejection does not even attempt to liken the cited claims to the recited structure of claims 1 and 12, let alone citing evidence and explaining the rejection. As such, the rejection is improper and should be withdrawn.

***5. Over claim 1 of Debregeas et al. (6,077,544)***

Claim 1 of the '544 patent reads as follows:

> 1. Spheroids comprising one or more active principles, with the exception of tiagabine, wherein said spheroids further comprise:
>
> a core and a layer coating said core, wherein said layer comprises at least one thermoplastic excipient which is of pasty to semi-solid consistency at a temperature of about 20° C., and whose melting point is between about 25 ° C. and about 100 ° C., coated with

> a flexible and deformable film, based on a polymer material, which ensures either protection or masking of the taste, or modified and controlled release of said one or more active principles, wherein said spheroids can be compressed directly without the addition of a substantial part of an auxiliary substance.

Here, the Examiner has not met her initial burden of establishing a prima facie case of ODP, Cf. In re Oetiker, 977 F.2d 1443, 1445, 24 U.S.P.Q.2d 1443, 1444 (Fed. Cir. 1992), because the Examiner ignores claim elements. For example, the rejection does not even attempt to liken the cited claims to the recited structure of claims 1 and 12, let alone citing evidence and explaining the rejection. As such, the rejection is improper and should be withdrawn.

***6. Over claim 1 of Debregeas et al. (6,139,877)***

Claim 1 of the '877 patent reads as follows:

> 1. Spheroids containing tiagabine as active principle and comprising:
>
> a core, or
>
> a core coated with a layer, said layer containing at least one thermoplastic excipient which is of pasty to semi-solid consistency at a temperature of about 20° C., and whose melting point is between about 25° C. and about 100° C.,
>
> said core or said layer being coated with
>
> a flexible and deformable film, based on a polymer material, whose glass transition temperature is less than about 30° C., which ensures either protection or masking of the taste, or modified and controlled release of the tiagabine.

Here, the Examiner has not met her initial burden of establishing a prima facie case of ODP, Cf. In re Oetiker, 977 F.2d 1443, 1445, 24 U.S.P.Q.2d 1443, 1444 (Fed. Cir. 1992), because the Examiner ignores claim elements. For example, the rejection does not even attempt to liken the cited claims to the recited structure of claims 1 and 12, let alone citing evidence and explaining the rejection. As such, the rejection is improper and should be withdrawn.

*7. Over claim 1 of DeBregeas et al. (6,228,395)*

Claim 1 of the '395 patent reads as follows:

> 1. Sustained-release (SR) microgranules containing Diltiazem which are free from water-soluble organic acid, comprising,
>
> a neutral granular support coated with an active layer comprising:
>
> Diltiazem or a pharmaceutically acceptable salt thereof as active principle,
>
> a surfactant, and
>
> a binder,
>
> a layer which ensures slow sustained release of the active principle (SR layer), and
>
> another active layer coating the SR layer, comprising:
>
> Diltiazem or a pharmaceutically acceptable salt thereof as active principle,
>
> a surfactant, and
>
> a binder,
>
> which is itself coated with an external layer which ensures rapid sustained release of the active principle contained in said another layer coating the SR layer.

Here, the Examiner has not met her initial burden of establishing a prima facie case of ODP, Cf. In re Oetiker, 977 F.2d 1443, 1445, 24 U.S.P.Q.2d 1443, 1444 (Fed. Cir. 1992), because the Examiner ignores claim elements. For example, the rejection does not even attempt to liken the cited claims to the recited structure of claims 1 and 12, let alone citing evidence and explaining the rejection. As such, the rejection is improper and should be withdrawn.

***8. Over claim 1 of Debregeas et al. (6,383,516)***

Claim 1 of the '516 patent reads as follows:

> 1. Sustained-release (SR) microgranules containing Diltiazem which are free from water-soluble organic acid, comprising
>
> (a) a core comprising:
>
> Diltiazem or a pharmaceutically acceptable salt thereof as active principle,
>
> a surfactant, and
>
> a binder,
>
> (b) a layer over the core (SR layer) that ensures slow sustained release of the active principle from the core,
>
> (c) an active layer coating the SR layer, comprising:
>
> Diltiazem or a pharmaceutically acceptable salt thereof as active principle,
>
> a surfactant, and
>
> a binder,
>
> which is itself coated with
>
> (d) an external layer which ensures rapid sustained release of the active principle contained in the active layer coating the SR layer.

Here, the Examiner has not met her initial burden of establishing a prima facie case of ODP, Cf. In re Oetiker, 977 F.2d 1443, 1445, 24 U.S.P.Q.2d 1443, 1444 (Fed. Cir. 1992), because the Examiner ignores claim elements. For example, the rejection does not even attempt to liken the cited claims to the recited structure of claims 1 and 12, let alone citing evidence and explaining the rejection. As such, the rejection is improper and should be withdrawn.

***9. Over claim 1 of Debregeas et al. (6,458,389)***

Claim 1 of the '389 patent reads as follows.

> 1. Controlled-release microgranules comprising (1) (a) a mixture comprising cisplatin and at least one pharmaceutically acceptable excipient or (b) a core of a neutral support grain coated with a mixture comprising cisplatin and at least one pharmaceutically acceptable excipient; and (2) a coating fixed to the microgranule, wherein the coating comprises a coating agent which enables the controlled release of the mixture; wherein the microgranules have a mean particle size of between 0.4 and 1.5 mm; and wherein the microganules contain only cisplatin as an active ingredient.

Here, the Examiner has not met her initial burden of establishing a prima facie case of ODP, Cf. In re Oetiker, 977 F.2d 1443, 1445, 24 U.S.P.Q.2d 1443, 1444 (Fed. Cir. 1992), because the Examiner ignores claim elements. For example, the rejection does not even attempt to liken the cited claims to the recited structure of claims 1 and 12, let alone citing evidence and explaining the rejection. As such, the rejection is improper and should be withdrawn.

***10. Over claim 1 of Debregeas et al. (6,482,437)***

Claim 1 of the '437 patent reads as follows:

> 1. An immediate-release microganule, each microgranule comprising a neutral support grain coated with a mixture of morphine sulfate and of a pharmaceutically acceptable binder, said binder representing 10 to 50% by weight of the morphine sulfate/binder mixture, and wherein said microgranule has a dissolution profile in water, buffered at a pH approximately equal to 7 and at a temperature of 37° C., by dissolution with a paddle at 100 revolutions/min, such that: more than 70% by weight of active principle is dissolved after 30 minutes, more than 90% by weight of active principle is dissolved after 60 minutes.

Here, the Examiner has not met her initial burden of establishing a prima facie case of ODP, Cf. In re Oetiker, 977 F.2d 1443, 1445, 24 U.S.P.Q.2d 1443, 1444 (Fed. Cir. 1992), because the Examiner ignores claim elements. For example, the rejection does not even attempt

to liken the cited claims to the recited structure of claims 1 and 12, let alone citing evidence and explaining the rejection. As such, the rejection is improper and should be withdrawn.

### *11. Over claim 1 of Debregeas et al. (6,551,621)*

Claim 1 of the '621 patent reads as follows:

> 1. Omeprazole microgranules, each comprising an active layer comprising the active principle and an external gastroprotective layer comprising a gastroprotective agent, characterized in that they are devoid of alkaline compounds in the form of salts and that the active layer comprises a hydrophobic substance.

Here, the Examiner has not met her initial burden of establishing a prima facie case of ODP, Cf. In re Oetiker, 977 F.2d 1443, 1445, 24 U.S.P.Q.2d 1443, 1444 (Fed. Cir. 1992), because the Examiner ignores claim elements. For example, the rejection does not even attempt to liken the cited claims to the recited structure of claims 1 and 12, let alone citing evidence and explaining the rejection. As such, the rejection is improper and should be withdrawn.

### *12. Over claim 1 of Debregeas et al. (6,660,296)*

Claim 1 of the '296 patent reads as follows:

> 1. Omeprazole microgranules, each comprising an active layer comprising the active principle and an external gastroprotective layer comprising a gastroprotective agent, characterized in that they are devoid of alkaline compounds in the form of salts and that the active layer comprises a hydrophobic substance.

Here, the Examiner has not met her initial burden of establishing a prima facie case of ODP, Cf. In re Oetiker, 977 F.2d 1443, 1445, 24 U.S.P.Q.2d 1443, 1444 (Fed. Cir. 1992), because the Examiner ignores claim elements. For example, the rejection does not even attempt to liken the cited claims to the recited structure of claims 1 and 12, let alone citing evidence and explaining the rejection. As such, the rejection is improper and should be withdrawn.

## Conclusion

It is believed that the present application is in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested.

The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check or credit card payment form being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicant hereby petitions for such extension under 37 C.F.R. § 1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

Date 07-05-2007

By _____

FOLEY & LARDNER LLP
Customer Number: 22428
Telephone: (202) 295-4166
Facsimile: (202) 672-5399

Sean A. Passino
Attorney for Applicants
Registration No. 45,943